

We claim:

1. A method for enhancing the stability of a triplex formed from one or more nucleic acid strands in a solution, said method comprising adding to the solution, either before or after formation of the triplex, an effective amount of either of the following:

(a) a water structure-making substance other than an alkali or alkaline earth metal cation, a

10 tetramethylammonium cation, or a polyamine; or

(b) a combination of said water structure-making substance and an alkali or alkaline earth metal cation, a tetramethylammonium cation, or a polyamine.

2. The method of claim 1 wherein the water structure-making substance comprises an organic cation other than tetramethylammonium.

3. The method of claim 2, wherein the organic cation is selected from the group consisting of methylammonium, dimethylammonium, trimethylammonium, and 20 tetraethylammonium.

4. The method of claim 1, wherein the water structure-making substance comprises a cationic lipid.

5. The method of claim 4, wherein the cationic lipid is selected from the group consisting of 25 cetyltrimethylammonium, tridodecylmethylammonium, and 2,3-dioleyloxy-N-[2(sperminecarboxamido)ethyl]-N,N-dimethyl-1-propanammonium.

6. The method of claim 1, wherein the water structure-making substance is selected from the group 30 consisting of dimethyl sulfoxide and poly(ethylene glycol).

7. The method of claim 1, wherein the water structure-making substance comprises an organic anion.

8. The method of claim 7, wherein the organic anion is acetate.

35 9. The method of claim 1, wherein the water structure-making substance comprises an inorganic anion.

10. The method of claim 9, wherein the inorganic

anion is selected from the group consisting of phosphate, sulfate, cyanate, isocyanate and isothiocyanate.

11. The method of claim 1, wherein the water structure-making substance comprises a water-miscible organic solvent.

12. The method of claim 11, wherein the water structure-making substance comprises an alcohol.

13. The method of claim 12, wherein the alcohol is selected from the group consisting of methanol, ethanol, isopropanol and 2-propanol.

14. The method of claim 1, wherein the third strand comprises DNA or RNA.

15. The method of claim 1, wherein the third strand comprises an unnatural heterocycle base substitute, a base analog, an unnatural backbone, or a substituent which strengthens binding of the third strand in the triplex.

16. A method for forming a triplex from one or more nucleic acid strands, said method comprising adding to a solution, in any order, the strand(s) and an effective amount of one of the following:

(a) a water structure-making substance other than an alkali or alkaline earth metal cation, a tetramethylammonium cation, or a polyamine; or

(b) a combination of said water structure-making substance and an alkali or alkaline earth metal cation, a tetramethylammonium cation, or a polyamine; and allowing said triplex to form.

17. The method of claim 16, wherein the water structure-making substance comprises an organic cation other than tetramethylammonium.

18. The method of claim 17, wherein the organic cation is selected from the group consisting of methylammonium, dimethylammonium, trimethylammonium, and tetraethylammonium.

19. The method of claim 16, wherein the water structure-making substance comprises a cationic lipid.

20. The method of claim 19, wherein the cationic

lipid is selected from the group consisting of cetyltrimethylammonium, tridodecylmethylammonium, and 2,3-dioleyloxy-N-[2(sperminecarboxamido)ethyl]-N,N-dimethyl-1-propanammonium.

5        21. The method of claim 16, wherein the water structure-making substance is selected from the group consisting of dimethyl sulfoxide and poly(ethylene glycol).

22. The method of claim 16, wherein the water structure-making substance comprises an organic anion.

10      23. The method of claim 22, wherein the organic anion is acetate.

24. The method of claim 16, wherein the water structure-making substance comprises an inorganic anion.

15      25. The method of claim 24, wherein the inorganic anion is selected from the group consisting of phosphate and sulfate.

26. The method of claim 16, wherein the water structure-making substance comprises a water-miscible organic solvent.

20      27. The method of claim 26, wherein the water structure-making substance comprises an alcohol.

28. The method of claim 27, wherein the alcohol is selected from the group consisting of methanol, ethanol, isopropanol and 2-propanol.

25      29. The method of claim 16, wherein the third strand comprises DNA or RNA.

30      30. The method of claim 16, wherein the third strand comprises an unnatural heterocycle base substitute, a base analog, an unnatural backbone, or a substituent which strengthens binding of the third strand in the triplex.

31. The method of claim 1, wherein the water structure-making substance is covalently linked to the third strand.

35      32. The method of claim 16, wherein the water structure-making substance is covalently linked to the third strand.